

REMARKS

The foregoing amendments cancels dependent claims 4 and 25, amends claims 1, 12, 15, 16, 20, 30, 32, 39, 40 and 43 and adds claims 46-48 to more fully claim the invention. Pending in the application are claims 1-48, of which claims 1, 12, 30, 32, 39, 40, 43, 46, 47 and 48 are independent. The following comments address all stated grounds for rejection and place the presently pending claims, as identified above, in condition for allowance.

Independent claims 1, 12, 30, 32, 39, 40 and 43 are amended to specify that each fluid interface port has a dead volume that is less than about 1 picoliter. Support for the amendment can be found throughout the application as filed, at least for example, in canceled claim 4, and on page 11, lines 4-14 of the specification.

Claim 15 is amended for purposes of clarity only to change the phrase "The separation of claim 12" to --The separation device of claim 12--.

Claim 16 is amended for purposes of clarity only to change the phrase "said reservoir layer" to --said array of cathode reservoirs and said array of anode reservoirs--.

Claim 20 is amended to delete the word "approximately" from line 2. *No new matter is added.*

Amendment and/or cancellation of the claims is not to be construed as an acquiescence to any of the objections/rejections set forth in the instant Office Action, and was done solely to expedite prosecution of the application. Applicant reserves the right to pursue the claims as originally filed, or similar claims, in this or one or more subsequent patent applications.

Objections to the Specification

Regarding the objection to the disclosure for lack of a definition of "N", Applicants have amended the specification on page 12, line 33 to define N as equal to the number of samples to be analyzed, as requested by the Examiner.

Objections to the Claims

Regarding the objection to claim 15 for omitting the word “device” in the preamble, Applicants have amended claim 15 to change the phrase “The separation of claim 12” to --The separation device of claim 12-- as requested by the Examiner.

Regarding the objection to claim 25 is objected for being exact duplicate of claim 13, Applicants have canceled claim 25, rendering the objection moot.

Claim rejections under 35 USC § 112

Regarding the rejection of claim 16 under 35 U.S.C. 112 for reciting the limitation “said reservoir array layer” in the second line of the claim without providing sufficient antecedent basis for this limitation in the claim, Applicants have amended claim 16 to change the phrase “said reservoir layer” to --said array of cathode reservoirs and said array of anode reservoirs--. These recitations have antecedent basis in lines 9-12 of claim 12.

Regarding the rejection of claim 20 under 35 USC 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention, Applicants have amended the claim to delete the word “approximately”, which the Examiner considers to render the metes and bounds of the claim unclear.

Claim rejections under 35 USC § 103

In the Office Action, the Examiner rejects claims 1-5, 7, 8, 12-26, 30-36 and 38 under 35 USC 103(a) as being unpatentable over Simpson *et al* in view of either Howitz *et al* or Arnold *et al*. The Examiner rejects claims 1 and 6 under 35 USC 103(a) as being unpatentable over Simpson *et al* in view of either Howitz *et al* or Bass. The Examiner rejects claims 9-11 and 27-29 under 35 USC 103(a) as being unpatentable over Simpson *et al* and either Howitz *et al* or Arnold *et al* as applied to claims 1 and 12 above, and further in view of Bjornson *et al*. Claim 37 is rejected under 35 USC 103(a) as being unpatentable over Simpson *et al* and either Howitz *et al* or Arnold *et al* as applied to claim 36 above, and further in view of Sundberg *et al*. Claim 39

is rejected under 35 USC 103(a) as being unpatentable over Simpson *et al* in view of Howitz *et al*. The Examiner also rejects claims 40-45 under 35 USC 103(a) as being unpatentable over Simpson *et al* in view of Howitz *et al*. Applicants respectfully traverse the rejection and submit that claims 1-45 distinguish patentably over the cited references. The cited references, alone or in combination, do not teach or suggest a separation device including one or more fluid interface ports, each having a dead volume of less than about one picoliter, formed in the side wall of a separation channel having a virtual wall formed by a separation medium disposed in the interior of the separation channel, as recited in independent claims 1, 12, 30, 32, 40 and 43.

The Simpson reference describes a capillary array electrophoresis (CAE) micro-plate including a plurality of cathode reservoirs and an anode reservoir. As recognized by the Examiner, the Simpson reference does not disclose fluid interface ports forming virtual walls. Rather, the Simpson reference discloses the use of *reservoirs* for providing sample to the separation channels in the CAE micro-plate.

The sample reservoirs and injection technique of Simpson have significant drawbacks, including significant amounts of wasted sample, as well as inefficient utilization of space and resources. For example, the sample reservoirs have a large footprint, resulting in a complicated and sizeable structure that is difficult and expensive to manufacture. The sample reservoirs have low injection efficiency, resulting in sample waste. In contrast to the claimed injection scheme, a larger amount of sample is inherently introduced from the sample reservoir to the separation channel than is necessary and must be reduced by separation. The indirect introduction of sample to a channel through the reservoirs also makes precise control of the sample injection difficult. In addition, the sample reservoirs increase the potential for sample pollution.

There is no teaching or suggestion in the Simpson reference that alternate means of sample introduction could be used in place of the cumbersome and inefficient reservoirs. In fact, the Simpson reference *requires* that the sample reservoirs be used, thereby teaching *away* from modifying the sample reservoirs. The reservoirs of Simpson are specifically designed to facilitate loading with a pipetter, which could not readily be used with the claimed fluid interface ports. The Simpson reference further teaches away from virtual wall fluid interface ports by indicating desirability of increasing the reservoir size in column 3, lines 12-21. Therefore, it

would be difficult and not obvious to change the sample reservoirs of Simpson to comprise the claimed virtual wall fluid interface ports.

The Examiner looks to the teachings of the Howitz reference and the Arnold reference to compensate for the deficiencies of the Simpson reference. However, even in combination, the references fail to anticipate the claimed invention. Moreover, Applicants respectfully submit that motivation to modify the teachings of the Simpson reference using the teachings of the Howitz reference and/or the Arnold reference is lacking.

The Howitz reference discloses a fluid microdiode for incorporating a dosed fluid into a target fluid contained in a closed system. According to the Examiner, because the Howitz device discloses a coupling surface for a flow channel comprising a grid of micromenisci, it would be obvious to modify the device of Simpson to include a fluid interface ports comprising holes through a side wall of a channel. The Examiner also considers the Arnold reference to disclose a device comprising a fluid interface port having a separation medium forming a virtual wall therein.

However, the menisci 6 formed in the microcapillaries of the device of Howitz do *not* comprise virtual walls, as set forth in the present application. Furthermore, the microcapillaries of Howitz do not have a dead volume that is less than about one picoliter. Rather, each microcapillary in Howitz has a volume that is significantly greater than one picoliter, due to the relatively large height of the microcapillaries. In contrast, the claimed fluid interface ports have a significantly smaller dead space, in part due to the smaller thickness of the side walls of the channel in comparison to the FMD chip of Howitz.

There is also no teaching or suggestion that the micromenisci of Howitz are “virtual walls” The term “virtual wall” is used to denote that the meniscus essentially replaces the removed portion of the side wall that forms the port. The word ‘virtual’ in the present claims refers to the effect that the overall liquid flow through the separation channel of the electrophoretic system is not influenced by the virtual wall, i.e. the flow of liquid in the micro-plate having a virtual wall is substantially identical to the flow of liquid through an identical micro-plate in which no virtual wall is formed. There is no teaching or suggestion in Howitz

that the micromenisci 6 essentially replace the side wall of the flow channel 7, or that the presence of the microcapillaries does not influence the flow of fluid through the flow channel.

The Arnold reference also does not teach or suggest the claimed fluid interface port. The access means 630 does not form a virtual wall when the associated channel is filled with a separation medium. In addition, there is no teaching or suggestion that the access means has a dead volume of less than one picoliter. Furthermore, the access means 630 merely provides internal access between two different channels in a substrate. Therefore, the access means 630 is not readily substitutable for the sample reservoirs of Simpson.

Furthermore, Applicants submit that motivation to combine references, a requirement in making a determination that a claim is obvious, is lacking. In determining whether a case of *prima facie* obviousness (“obvious on its face”) exists, it is necessary to ascertain whether the prior art teachings would appear to be sufficient to one of ordinary skill in the art to suggest making the claimed substitution or other modification. The prior art must provide the motivation to make a change to its own teachings to arrive at the invention under rejection. That is, it is not sufficient that the prior *could be* so modified; instead the prior art must teach or suggest that the prior art *should be* so modified.

Under U.S. law, even if a combination of the references teaches every element of the claimed invention, without a motivation to combine, a rejection based on a *prima facie* case of obvious is improper. The Examiner has not pointed to an objective reason to modify the teachings of the Simpson reference using the teachings of the Howitz reference or the other cited references. Therefore, the *prima facie* case of obviousness has not been made and the Examiner’s rejection is improper. As is evident from a close reading of the references and a comparison to the pending claims, the instant rejection of claims 1 and 3 constitutes nothing more than a picking and choosing of the various elements of the claims from a number of references based, not on motivation from the references themselves, but rather based on the teachings of the application. Thus, the instant rejection constitutes an impermissible hindsight reconstruction of the invention.

Even so, the claims are patentable over the references, because neither reference describes a fluid interface port having a dead volume that is less than one picoliter, as recited in independent claims 1, 12, 30, 32, 39, 40, 43 and 46-48. As set forth in the present application, “dead volume” refers to the volume of liquid retained in the fluid interface port (i.e. the volume of liquid the fluid interface port holds that is not flushed through the fluid interface port by the flow field of liquid through the microchannel). The relatively small dead volume provided by the virtual wall results in a direct fluid interface allowing direct injection of a precise volume of sample into the interior of the microchannel from the exterior of the microchannel. The ability to directly inject sample into the microchannel due to the low dead volume of the fluid interface port provides improved control over the amount of sample that is injected into the microchannel, allows efficient use of sample, and significantly reduces waste of the sample. Furthermore, the direct injection provided by the very small dead volume reduces or prevents cross-contamination between different samples and allows a second substance to be directly injected into the system immediately after a first substance without requiring flushing of the fluid interface port. As described above, the cited references, alone or in combination, do not teach or suggest a fluid interface port having a dead volume that is less than one picoliter. Therefore, claims 1-48 are patentable and in condition for allowance.



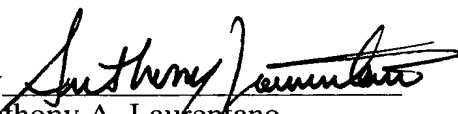
CONCLUSION

In view of the above amendment, Applicants believe the pending application is in condition for allowance, and request that the Examiner pass the application to allowance.

Applicants believe no fee is due with this statement. However, if a fee is due, please charge our Deposit Account No. 12-0080, under Order No. TGZ-007 from which the undersigned is authorized to draw.

Dated: December 9, 2004

Respectfully submitted,

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